

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: P. HUSK

National Stage of PCT/EP00/00319

Group Art Unit: Unassigned

Filed: July 18, 2001

Examiner: Unassigned

For: GENETIC PREDISPOSITION

Attorney Docket No.: 8969-029

PRELIMINARY AMENDMENT

Box PATENT APPLICATION

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Please enter the following amendments and remarks into the file of the above-identified application prior to the examination thereof.

IN THE SPECIFICATION

Marked up versions of all paragraphs showing insertions and deletions are included in Appendix A.

Please replace the paragraph starting at page 1, line 5 with the following text:

--TECHNICAL FIELD

This invention relates to a method for assessing predisposition to various conditions based upon polymorphisms in a bone sialoprotein gene, a matrix gla protein gene, an osteopontin gene and/or an osteoprotegerin (OPG)/osteoclastogenesis inhibitory factor (OCIF) gene. More specifically, the invention relates to a method of assessing an individual's predisposition to various pathological calcification conditions including osteoporosis and atherosclerosis by screening for these polymorphisms. The method of the present invention is especially useful in determining allelic variations in the human bone sialoprotein gene, the human matrix gla protein gene, the human osteopontin gene and/or the

osteoprotegerin (OPG) /osteoclastogenesis inhibitory factor (OCIF) gene thus predicting predisposition to high or low bone mineral density (BMD). The invention also relates to bone sialoprotein (BSP) genes, matrix gla protein (MGP) genes, osteopontin (OPN) genes and OPG/OCIF genes containing the polymorphisms and to probes and primers therefor.--

Please replace the paragraph starting at page 5, line 16 with the following text:

--SUMMARY OF THE INVENTION

The present invention now provides a method of assessing an individual's predisposition to a selected calcification condition status, which method comprises determining the genotype of the promoter of the bone sialoprotein gene, the promoter of the matrix gla protein gene, the promoter of the osteopontin gene, or the promoter of the OPG/OCIF gene or all four or any combination of two or more out of the four promoters.--

Please replace the paragraph starting at page 17, line 6 with the following text:

--BRIEF DESCRIPTION OF THE DRAWINGS

In order that the nature of the present invention be more clearly understood, there now follows an example in which reference is made to the Figures shown in the accompanying drawings in which: --

Please replace the paragraph starting at page 22, line 13 with the following text:

--DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

Example 1 (18 year study)

Methods

Subjects. One hundred thirty three women followed up for 18 years (1977-1995) with respect to BMD, biochemical markers, height, and weight were used in the study. A detailed description of the cohort has been previously published (Jorgensen et al., 1996).--

IN THE CLAIMS

Please rewrite claims 3, 14, 23, and 24 to recite.:

A list of changes to the claims showing insertions and deletions is provided herewith as Appendix B.

3. (Amended once) A method as claimed in Claim 1, wherein it is determined whether the individual is homozygous or heterozygous for an allelic variation of the promoter of the bone sialoprotein gene, the promoter of the matrix gla protein gene, the promoter of the osteopontin gene or the promoter of the OPG/QCIF gene, or all four or a combination of two or more out of the four promoters.

14. (Amended once) A method as claimed in Claim 1, comprising amplifying a relevant portion of the DNA of a said gene promoter of said individual.

23. (Amended once) A method of osteoporosis therapy comprising determining a predisposition as claimed in Claim 1, and administering a medicament to the individual to prevent or treat osteoporosis or to delay the onset of osteoporosis if the individual is predisposed to low peak bone mass or to a high rate of loss of bone mass.

24. (Amended once) A method of atherosclerosis therapy comprising determining a predisposition as claimed in Claim 1, and administering a medicament to the individual to prevent or treat atherosclerosis or to delay the onset of atherosclerosis if the individual is predisposed to pathological arterial calcification.

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REMARKS

Claims 1-24, as amended, are pending in this application for the Examiner's review and consideration. Applicants have amended the specification and claims to conform with U.S. patent practice and to more clearly recite the invention. Claims 3, 14, 23, and 24 were amended so that they are not multiple dependent claims. As no new matter has been added herein, these changes should be entered.

Date

July 18, 2001

Respectfully submitted,

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